

REMARKS

This paper is being filed in response to the Office Action dated June 3, 2003 that was issued in the above-identified application. Applicants respectfully request continued examination of the instant application pursuant to 35 U.S.C. §132(a) and 37 C.F.R. §1.114(a)(2) and enclose herewith the fee required pursuant to 37 C.F.R. §1.17(e). Applicants also request a three-month extension of time and enclose the fee required under 37 C.F.R. §1.17(a)(3). Applicants further enclose herewith a Third Substitute Sequence Listing in paper and computer readable form in accordance with 37 C.F.R. §§ 1.821 to 1.825 and a Terminal Disclaimer under 37 C.F.R. § 1.321(b). Applicants respectfully request reconsideration of the above-identified application in light of the amendments and remarks presented in the instant Amendment.

Claims 42-51, 53, 55-56, 82, and 85-86 are pending. Claims 42-45, 53, and 55 have been amended. Dependent claim 42 has been amended to correspond to independent claim 43 and to recite "isolated or purified". Independent claim 43 has been amended to correspond to dependent claim 42. Claims 44-45 and 55 have been amended to refer to claim 42 instead of claim 43. Therefore, these amendments do not constitute new matter. Amended claim 53 is supported by the specification as originally filed, for example, by Example 10 and, therefore, does not constitute new matter. Upon entry of the instant Amendment, claims 42-51, 53, 55-56, 82, and 85-86 will continue to be pending.

As a preliminary matter, Applicants thank the Examiner for granting Applicant's request to shift the elected species. Applicants also thank the Examiner for withdrawing many of the previous rejections to the claims including rejections that the claimed invention lacks utility, constitutes new matter, is not enabled by the specification, is indefinite, and is anticipated by Halpern (1993, *JBC* 268:11186-11192) and Kink (U.S. Patent No. 5,736,139).

Amendments Are Fully Supported

The specification has been amended to recite Accession Nos. X52066 and M81186. This amendment is supported by the specification as originally filed. For example, the specification originally cited Thompson et al., 1990, *European Journal of Biochemistry* 189:73-81 at page 12, lines 9-10. The botulinum neurotoxin serotype A sequence disclosed in Figure 3 (pp. 76-77) of this document was deposited in Genbank and assigned Accession No. X52066. See Accession No. X52066 (annotations recite Thompson et al. as the only “reference”)(Exhibit 1). Additionally, the specification originally cited Whelan et al., 1992, *Applied and Environmental Microbiology* 58:2345-2354 at page 13, line 1. This article recites Accession No. M81186 at page 2346, second column, second full paragraph.

SEQ ID NOS: 7, 37, 39, 40, 41, and 42 have been amended herein. SEQ ID NO:7 has been amended to agree with Figure 4 as originally filed with the instant application. Therefore, this amendment does not constitute new matter.

SEQ ID NO:37 has been amended to correspond to the sequence shown in Figure 2 of U.S. Patent Application No. 08/123,975 by Middlebrook et al. filed on September 21, 1993 (hereinafter “the ‘975 application”) and to which the instant application claims priority. Therefore, this amendment does not constitute new matter.

SEQ ID NO:39 has been amended to correspond to the sequence shown in Figure 4 of the ‘975 application. Therefore, this amendment does not constitute new matter.

SEQ ID NO:40 has been amended to agree with Figure 3 on page 2349 of Whelan (Accession No. M81186)(hereinafter “Whelan”). SEQ ID NO:41 has been amended to agree with Figure 3 on pages 76-77 of Thompson (Accession No. X52066)(hereinafter “Thompson”). SEQ ID NO:42 has been amended to agree with Whelan. Applicants assert that Thompson and

Whelan were available to those of ordinary skill in the art at the time the instant application was filed. Specifically, the National Center for Biotechnology Information indicates that Thompson was “first seen” on April 21, 1993 (Exhibit 1) and Whelan was “first seen” on April 26, 1993 (Exhibit 2). In addition, the specification has been amended to specifically incorporate Thompson and Whelan by reference. In this regard, Applicants respectfully invite the Examiner's attention to page 44, line 18-20 of the specification, which states “All publications and patent applications are herein incorporated by reference to the same extent as if each individual publication or patent application was specifically and individually indicated to be incorporated by reference..” Therefore, these amendments do not constitute new matter.

Declarations

Applicants submit herewith a Third Substitute Sequence Listing in paper and computer readable form. I hereby state that the content of the paper and computer readable copies of the Third Substitute Sequence Listing submitted in accordance with 37 C.F.R. §1.821(c) and (e), are the same. I hereby state that the content of the paper and computer readable copies of the Third Substitute Sequence Listing, submitted in accordance with 37 C.F.R. §1.821(g), herein does not include new matter.

Applicants Third Substitute Sequence Listing corrects typographical errors in the sequences presented in the original application and in the Amendment and Substitute Sequence Listing filed on March 5, 2002. Applicants enclose herewith six sequence alignments for the Examiner's review. The original sequence, the sequence substituted on March 5, 2002 (hereinafter “the Substitute sequence”), and the sequence as amended herein (hereinafter “the Amended sequence”) are aligned along with the sequence relied upon to support the instant amendment. Positions where the sequences differ are highlighted, while positions where all

aligned sequences match are marked with an asterix. These alignments have been prepared with ClustalW 1.74 accessed at <<http://www.ch.embnet.org/software/ClustalW.html>> with default settings.

Applicants have amended the specification to incorporate the Thompson and Whelan sequences in the sequence listing respectively as SEQ ID NOS:43 and 44. Both Thompson and Whelan sequences were incorporated by reference into the instant application. *See* page 44, lines 18-20. I hereby declare that SEQ ID NO: 40, as amended herein, is the same as Whelan amino acids 853 to 1291. I hereby declare that SEQ ID NO: 41, as amended herein, is the same as Thompson amino acids 449 to 1296. I hereby declare that SEQ ID NO: 42, as amended herein, is the same as Whelan amino acids 442 to 1291.

Claims Are Arranged in Proper Sequence

Claim 42 has been objected to as allegedly depending on a later claim. Applicants have amended claim 42 to replace claim 43 and vice-versa. Therefore, upon entry of the instant amendment, claims 42 and 43 will be in proper sequence. Applicants, therefore, respectfully request withdrawal of this objection.

Claims Relate to Patentable Subject Matter

Claims 42-43, 45-47, and 55-56 have been rejected under 35 U.S.C. § 101 as allegedly directed to non-statutory subject matter. The Examiner has alleged that natural variation in nucleotide and amino acid levels for the same or equivalent proteins is common in nature.

Applicants traverse this rejection and assert that the claims, as amended herein, are drawn to patentable subject matter. Applicants, therefore, respectfully request withdrawal of this rejection.

Claims Are Supported By Adequate Written Description

Claims 42-51, 53, 55-56, 82, and 85-86 have been rejected under 35 U.S.C. § 112, first paragraph as allegedly lacking sufficient written description. The Examiner has alleged that Example 7 and Figure 2 do not define a representative number of species of the instantly claimed genus of nucleic acid molecules.

Applicants traverse this rejection and assert that the claims, as amended herein, are supported by an adequate written description. The Examiner has alleged that the phrase "a nucleic acid comprising a nucleic acid sequence" encompasses variant nucleic acid sequences. This phrase has been omitted. Applicants, therefore, respectfully request withdrawal of this rejection.

Claims Are Clear and Definite

Claim 43 has been rejected under 35 U.S.C. § 112, second paragraph as allegedly indefinite in reciting "said amino acid sequence comprising at least one immunogenic epitope". The Examiner has alleged that it is unclear whether the immunogenic epitope is inherent to SEQ ID NO:4 or heterologous to SEQ ID NO:4 since the term "having" is construed to be open.

Applicants traverse this rejection and assert that it is clear that the immunogenic epitope is part of SEQ ID NO:4. Claim 42 has been amended to replace claim 43 and vice-versa. Applicants respectfully submit that the antecedent basis for the phrase "said amino acid sequence comprising at least one immunogenic epitope" recited in claim 42 is the immediately prior

phrase, namely, “the amino acid sequence of SEQ ID NO:4” (emphasis added). Thus, it is clear that the immunogenic epitope is part of SEQ ID NO:4. Accordingly, Applicants respectfully request withdrawal of this rejection.

Claim 53 has been rejected under 35 U.S.C. § 112, second paragraph as allegedly indefinite. The Examiner has alleged that the method steps are not commensurate in scope with the preamble.

Applicants traverse this rejection and assert that claim 53, as amended herein, is clear and definite. Both the preamble and the method step recite “isolating.” Applicants, therefore, respectfully request withdrawal of this rejection.

Specification and Claims Are Free of New Matter

Applicant’s Preliminary Amendment and Substitute Sequence Listing mailed on March 5, 2003 has been objected to under 35 U.S.C. § 132 as allegedly introducing new matter.

1(a). SEQ ID NO:3

Claim 42 has been rejected under § 112, first paragraph as allegedly containing new matter in reciting “nucleotides 13-1314”. The Examiner has alleged that there is no descriptive support for this subfragment of SEQ ID NO:3.

Applicants traverse this rejection and respectfully assert that the specification as originally filed supported this fragment of SEQ ID NO:3. Applicants respectfully invite the Examiner’s attention to Figure 2 and note that SEQ ID NO:3 is depicted almost exclusively in upper case letters. The only exceptions are the “atg” at positions 13-15 and the “taa” at positions 1315-1318. Applicants assert that it would have been abundantly clear to one of ordinary skill in the art that these lower case letters refer to the start codon (atg) and the termination codon (taa).

Therefore, since the stop codon does not encode an amino acid, one of ordinary skill in the art would have trouble understanding that nucleotides 13-1314 are the amino acid-encoding nucleotides of SEQ ID NO:3. Accordingly, Applicants respectfully request withdrawal of this rejection.

1(b). SEQ ID NO:37

The Examiner has alleged that Figures 1, 2, and 3 do not support the amendments to SEQ ID NO:37. Without acquiescing in this rejection, Applicants have amended SEQ ID NO:37 to correct errors. This amendment is supported by Figure 2 of the '975 application to which the instant application claims priority.

2. SEQ ID NOS: 7 and 39

The Examiner has alleged that Figure 4 (SEQ ID NO:7) do not support the amendments to SEQ ID NO:39 and vice versa. Without acquiescing in this rejection, Applicants have amended SEQ ID NOS: 7 and 39 to correct errors. These amendments are respectively supported by the original Figure 4 submitted with the instant application and Figure 4 of the '975 application.

3. SEQ ID NO:40

The Examiner has alleged that Accession No. M81186 and SEQ ID NO:8 do not support the amendments to SEQ ID NO:40. Without acquiescing in this rejection, Applicants have amended SEQ ID NO:40 to correct errors. This amendment is supported by Figure 3 of Whelan (Accession No. M81186), which was incorporated by reference into the instant application.

4. SEQ ID NO:41

The Examiner has alleged that Figures 1, 2, and 3 and SEQ ID NO:38 do not support the amendments to SEQ ID NO:41. Without acquiescing in this rejection, Applicants have amended SEQ ID NO:41 to correct errors. This amendment is supported by Figure 3 of Thompson (Accession No. X52066), which was incorporated by reference into the instant application.

5. SEQ ID NO:42

The Examiner has alleged that Figure 4 (SEQ ID NO:8) and Accession No. M81186 do not support the amendments to SEQ ID NO:42. Without acquiescing in this rejection, Applicants have amended SEQ ID NO:42 to correct errors. This amendment is supported by Figure 3 of Whelan (Accession No. M81186), which was incorporated by reference into the instant application.

Thus, all of the amendments to the sequence listing are fully supported and, therefore do not constitute new matter. Applicants, therefore, respectfully request withdrawal of this rejection.

Claims Do Not Represent Double Patenting

Claims 45, 48, 53, and 82 have been rejected under the judicially-created doctrine of obviousness-type double patenting as allegedly obvious over U.S. Patent No. 6,495,143 issued to Lee JS et al. on December 17, 2002. The Examiner indicated that a timely filed terminal disclaimer would overcome this rejection.

Applicants respectfully invite the Examiner's attention to the Terminal Disclaimer enclosed herewith. A copy of the executed Assignment is also enclosed herewith.

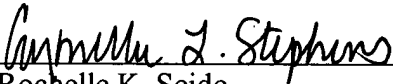
In summary, Applicants believe that all pending claims are in condition for allowance and respectfully solicit prompt favorable action.

Applicants enclose herewith the fee required under 37 C.F.R. §1.17(e) and §1.17(a)(3). Although Applicants do not believe that any additional fees are required with this paper, the Commissioner is hereby authorized to charge any fees occasioned by this submission not otherwise enclosed herewith to Deposit Account No. 02-4377. Please credit any overpayment of fees associated with this filing to the above-identified deposit account. A duplicate of this page is enclosed.

Respectfully submitted,

BAKER BOTTS, L.L.P.

December 3, 2003



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Enclosures

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Cost Code (Acct. Use Only):	P - PATENT FILING FEE
Patent Coupon Book:	n/a
Description: Filing Fee for	P19 - Other (Details Listed Below)
P13 Details:	Months Needed: 3
P19 Details:	Other: Request for Continued Examination
P37 Details:	PCT Application Designating the Following:
Voucher No. (Acct. Use Only):	
Check No. (Acct. Use Only):	
Bank No. (Acct. Use Only):	05 - NEW YORK OPERATING